SCIENTIFIC ABSTRACT

TITLE: Phase I Study of Percutaneous Injection of Adeno-virus P53 Construct (Adeno-p53)for Hepatocellular Carcinoma (UPCI #96-035)

The objectives of this study are to determine the safety of percutaneously delivered, intralesionally injected adeno-virus p53 construct (adeno-p53) in patients with hepatocellular carcinomas (HCC), and to investigate the potential anti-tumor effects of intralesional adeno-p53 given by monthly percutaneous injections.

Potential antitumor tumor effects will be explored by examining relationships among tumor response, incorporation and expression of the traduced gene, degree of apoptosis, and degree of p53 immune response. Because there are likely to be few samples with which to examine these relationships, this analysis will be exploratory in nature. It is expected that these results will be useful in generating hypotheses and in planning future studies of this treatment.

This is a Phase I study of intralesional injection of adeno-p53 in patients with hepatocellular carcinoma. Three patients will be initially entered at each dose level. If none of these patients develops grade 3 non-hematologic toxicity or grade 4 hematologic toxicity, escalation to the next dose will proceed. If one patient out of the 3 entered in a cohort develops such toxicity, 3 more patients will be entered at that dose level. If 2 of the 6 patients develop toxicities as above, this dose will be the maximum tolerated dose (MTD) and further dose escalations will cease. The dose level below the MTD will be the maximum acceptable dose (MAD), which will be utilized for Phase II studies. Six patients will be entered at the MAD, even if it is necessary to enroll 3 patients at that dose after the MTD has been identified. It will, therefore, be possible to confirm that 0 or 1 patients out of 6 have unacceptable toxicity at the MAD. The MTD and MAD will be defined.

One to two evaluable or measurable sites of disease will be selected in each patient for treatment. Factors which will be used by the investigator to select the lesions for treatment (indicator lesions) include ease of access, ease of biopsy, measurability, and safety of the injection approach.

Study treatment will be repeated monthly. A course is defined as Day 1 through Day 28 ($\pm$ 5 days) of study treatment. In case of a significant adverse event(s), study treatment may be delayed up to 2 weeks, until all adverse events have recovered to at least grade 1 or baseline level (which ever is higher).

Study treatment will continue as long as there is no tumor progression, no unacceptable adverse events, and no additional anticancer therapy is required. After a patient has completed six courses of study treatment and shown tolerance and clinical benefit, the patient will be evaluated to determine eligibility for continuation of therapy, subject to study material availability.